

Brain Fog: Does Air Pollution Make Us Less Productive?

Silke Schmidt

<https://doi.org/10.1289/EHP4869>

The regulation of air pollution has reduced its toll on heart and lung diseases. For example, the Clean Air Act Amendments of 1990 helped avert an estimated 160,000 deaths and 86,000 hospitalizations in 2010 alone.¹ However, a growing body of research suggests that polluted air also puts our brain in harm's way.

Chronic exposure to traffic-related pollutants may increase the risk of neurological disorders.² Both short- and long-term exposures have been associated with reduced human capital, including the academic performance of schoolchildren³ and the productivity of workers across the adult lifespan.⁴ As Matthew Neidell of Columbia University and Joshua Graff Zivin of the University of California, San Diego, wrote in 2018, “The ubiquity of these less lethal impacts, revealed by emerging economic research on labor productivity and human capital accumulation, ... can add up to considerable, society-wide impacts across the globe.”⁴

Components of Outdoor and Indoor Air Pollution

Estimating the subtle effects of air pollution requires long-term air quality data. The Clean Air Act has made much of this

information available to researchers and the general public through an extensive monitoring network for selected outdoor air pollutants. Today, this national network⁵ contains more than 4,000 monitoring stations operated mainly by state environmental agencies. These agencies send hourly or daily measurements of pollutant concentrations to a central database maintained by the U.S. Environmental Protection Agency (EPA).

The U.S. EPA defines and monitors six “criteria pollutants” in ambient air: particulate matter (PM), ground-level ozone, sulfur dioxide, nitrogen dioxide, carbon monoxide, and lead. PM includes a variety of tiny airborne solids and droplets emitted by vehicles, factories, wildfires, and other anthropogenic and natural sources. Additional pollutants from outdoor sources include methane, volatile organic compounds (VOCs), pollen, metals, and other sulfur and nitrogen oxides.

Although generated outdoors, these chemicals can travel indoors, where people spend a lot of their day—Americans, for example, spend on average 90% of their time inside.⁶ Concentrations of outdoor pollutants are lower inside than outside. But Joseph Allen, an assistant professor of exposure



Pollutants generated outdoors can travel indoors, where Americans spend on average 90% of their time. Some of the energy-efficient building practices introduced in the 1970s allowed indoor pollutants to concentrate; by the 1980s, reports of “sick building syndrome” had begun to appear in the medical literature.⁵² Newer building rating systems such as Leadership in Energy and Environmental Design® recognize the importance of optimal ventilation.⁵³ Image: © Pavel L. Photo and Video/Shutterstock.

assessment science at Harvard University, points out the “dirty secret” of outdoor air pollution. “When we account for the time we spend in buildings, a simple calculation shows that the majority of our exposure to outdoor air pollution can actually occur indoors,” he explains. The extent of penetration depends on building construction, ventilation rates, local meteorology, and the pollutant itself. Another factor is whether outdoor temperatures call for open windows.

Indoor sources also generate a mix of pollutants. For instance, PM is generated by cooking and home heating. Common indoor allergens include molds and the feces, saliva, and body parts of dust mites and cockroaches. And VOCs, which evaporate at low temperatures, are emitted by building materials, paints and protective coatings, adhesives in carpets and furniture, cleaning agents, and other products.

Air pollution travels the other way, too. Researchers recently estimated that, with declines in outdoor sources of some pollutants, VOCs from indoor uses of chemical products now make up a larger proportion of outdoor organic air pollution than they used to in urban areas.⁷

That discovery was a game changer for the relative importance of VOCs, according to Allen. “We should not be thinking of them only as an indoor concern,” he says. “In addition to the dirty secret of outdoor air pollution, we now have a dirty secret of indoor air pollution, too.”

According to the 2018 *State of Global Air* report,⁸ an estimated 95% of the world’s population breathes unhealthy ambient air, with annual fine PM (PM_{2.5}) concentrations above the World

Health Organization standard of 10 µg/m³. The report found the combination of outdoor PM_{2.5}, household air pollution, and ozone to be the fourth-leading human health risk factor globally. These three pollutants account for an estimated 11.2% of deaths in the world.

The ubiquity of polluted air has motivated researchers from many different fields to study not only its effects on mortality and morbidity, but also its more subtle effects on the healthy brain.

Short-Term Effects of Air Pollutants on the Brain

When Columbia’s Matthew Neidell, a professor of health policy and management, began to study air pollution and human productivity, he started with people who work primarily outdoors (fruit pickers in California⁹). He then followed with studies of indoor workers in the manufacturing industry (pear packers in California¹⁰) and white-collar office workers in the service sector (call center employees in China¹¹).

Neidell’s team saw consistent evidence that higher levels of outdoor air pollution was associated with decreased worker output. But they also saw an association in call center employees. “We found that they were completing fewer calls and taking more breaks on days with high air pollution,” Neidell says. He speculates that workers perhaps “just felt a little bit off without really knowing why and stepped away from their desk to go to the bathroom or the water cooler more often.”

This may sound small, but the potential economic impact can be substantial. For example, in 2014, the U.S. EPA’s Air Quality



Government regulation and emission reduction technology for vehicles and factories have decreased emissions from certain point sources of outdoor air pollution. VOCs that escape from indoor uses of chemical products now make up a greater share of outdoor organic air pollution in urban areas.⁷ Image: © iStockphoto/cgering.

Index in Los Angeles County exceeded 150 (a score considered “unhealthy for the general population”) on 28 days.¹² If the estimated association between air quality and productivity in Chinese call workers applied to all workers in service industry jobs in Los Angeles County, the authors projected that reducing air pollution to index values below 150 would generate an increase in the sector’s productivity of more than \$370 million.¹¹

To explore whether PM_{2.5} might influence cognitive functions, Neidell and his team turned to the New York Stock Exchange.¹³ Analyzing 10 years of S&P 500 returns as a proxy for the job performance of stockbrokers, they found that higher ambient PM_{2.5} levels in New York City were associated with reduced stock trading returns. No such association was found between the stock market and air quality in any of 43 other major U.S. cities.

To interpret this finding, Neidell points to studies suggesting that lower cognitive ability may lead to more risk-averse behavior.^{14,15} “For stockbrokers, that might mean their decisions shift toward less risky investments,” he speculates.

A widely used proxy for market risk aversion,^{16,17} known as the “fear index,” was also correlated with New York’s PM_{2.5} levels in Neidell’s study, supporting his hypothesis. The relationship with the S&P 500 was surprisingly strong; for example, an increase in particle pollution of one standard deviation was associated with an 11.9% reduction in same-day returns.

The findings have wide-ranging implications because “stock price variations send investment signals across the whole of the U.S. and international economy,” the authors wrote.¹³ A similar association was reported for more than 100,000 investors at a German brokerage firm.¹⁸

To follow up on these intriguing results, Neidell is now doing a campus-based study. He is testing whether the decision-making ability of Columbia University students varies with outdoor PM_{2.5} levels, as measured at the building where the students are assessed.

This approach is moving in the direction of a recent study¹⁹ of indoor air pollutants led by Allen. Similar in spirit to an experimental study of traffic pollution in 1970,²⁰ it randomly assigned different pollutant and ventilation levels to participants in an office, then asked them to complete a cognition test at the end of the day. The participants and the analysts who scored their tests were blinded to exposure status, and each person was his or her own control.

Test scores were significantly higher in room conditions with lower VOC levels. The researchers reported similar results for relatively low levels of carbon dioxide (CO₂), a marker of ventilation long thought to be benign at typical indoor concentrations. A later study by Allen’s team found that airline pilots performed better during advanced maneuvers (like flying with only one engine in a flight simulator) when exposed to lower amounts of CO₂, compared with higher exposures.²¹ This finding further supports the role of CO₂ as a potential indoor pollutant.²²

In the original study of office workers,¹⁹ test scores in low-VOC/low-CO₂ rooms were even higher with increased ventilation rates. Allen’s team estimated the cost of increasing building ventilation standards from the current 20 cubic feet per minute per person (cfm/p) to 40 cfm/p across a range of U.S. climate zones. The researchers projected that the additional annual energy costs would be at most \$40 per person, but that companies would gain \$6,500 per employee from greater productivity.²³



Evidence points to the subtle impact that air pollution may have on employee productivity. One team reported an association between higher ambient PM_{2.5} levels and reduced stock trading returns, perhaps due to greater risk aversion. Image: © iStockphoto/kasto80.

“Clearly, the [estimated] benefits of improved health and human productivity vastly overwhelm the costs,” Allen says. “For too long, the focus has been on energy efficiency, and health has been left out of the equation. But the two concepts really are not a mutually exclusive proposition.”

Other studies, mostly of outdoor pollutants, are consistent with Allen’s reports that short-term exposures may impair healthy brain function—not only that of working-age adults in office buildings and airplanes, but also of schoolchildren.

For example, researchers led by Jordi Sunyer, a professor of preventive medicine and public health at Pompeu Fabra University in Barcelona, Spain, found that increases in daily ambient levels of traffic-related air pollution were associated with reduced attention spans of primary schoolchildren.²⁴ In Israel, higher daily PM_{2.5} levels were associated with reduced performance by high school students on the high-stakes Bagrut exam, which impacts college admission.³ Higher exam-day PM_{2.5} levels also were associated with fewer years of post-secondary education and reduced monthly earnings, based on follow-up at 28–30 years of age.³

Long-Term Effects of Air Pollutants on the Brain

Other studies have investigated the effect of chronic fetal and childhood exposures. Frederica Perera’s group at Columbia University conducted pioneering work in this area, demonstrating that prenatal exposure to airborne polycyclic aromatic hydro-

carbons was associated with cognitive developmental delay at 3 years of age.²⁵

Other studies have associated prolonged exposure to air pollutants *in utero* or during childhood with reduced academic performance,^{26,27,28} a greater risk of autism spectrum disorder,^{29,30} and lower adult earnings.³¹ For older adults, most studies of long-term exposure have found associations with cognitive decline and neurodegenerative diseases.^{2,32}

Spanning a wide range of ages, a recent panel study in China caught the attention of scientists and mainstream media outlets alike. In a nationally representative sample of more than 25,000 children and adults in 162 counties, a higher air pollution index was associated with reduced cognitive function, with stronger impacts estimated for long-term (up to 3 years) than short-term (1- to 7-day) exposures.³³

The researchers correlated math and verbal scores from two county-level test waves (in 2010 and 2014) with data from 402 air quality monitoring stations in Chinese cities. Overall, the pollutant levels were higher than in the United States and Europe but comparable to other parts of the developing world.

In the United States, a study of this scale—a large sample size with a wide range of ages and highly variable exposures, but the same cognitive assessment—will not be possible anytime soon, says Jiu-Chiuan Chen, an associate professor of preventive medicine at the University of Southern California. But the Chinese findings of a stronger association in older and less educated men could be echoed in U.S. populations, despite lower levels of air pollution in American cities.



Studies have shown negative associations between air pollution levels and test performance. Poor performance on high-stakes tests and entrance exams can have long-term implications for a student’s earning potential.³ Image: © Hero Images.

“We’ve seen similar evidence for sexual dimorphism and socioeconomic disparities in neurotoxicity in our own study,” says Chen. “Higher PM_{2.5} exposure in Southern California²⁸ was associated with reduced intelligence in adolescents and young adults, with a stronger [association] in males and families of lower socioeconomic status.”

In their study, the authors measured IQ scores with the Wechsler Abbreviated Scale of Intelligence.²⁸ The potential effect modification by sex or social class is a newer finding, but Chen points out that the Chinese study is a compelling corroboration of research that Lilian Calderón-Garcidueñas conducted in a highly polluted environment more than 15 years ago. Now at the University of Montana in Missoula, she was the first scientist to link air pollution and neurodegeneration in the early 2000s, starting with the brains of dogs in Mexico City³⁴ and followed by studies of children³⁵ and adults³⁶ that continue to this day.

Biological Mechanisms: The Neurotoxicity of Urban Air Pollution

The pioneering work of Calderón-Garcidueñas inspired Michelle Block’s interest in the mechanisms by which air pollutants damage the brain. Back in 2002, Block’s postdoctoral advisor warned her that this topic would be “much dirtier” than studying a single metal or herbicide. This, in a nutshell, described the greater challenge of determining which specific component of urban air pollution harms which cell type, as both PM_{2.5} and VOCs are highly complex mixtures of many different chemicals.

However, the warning did not deter Block, who is now an associate professor of anatomy and cell biology at Indiana University. Yet many years later, she says, we still do not know exactly what gets into the brain and through which biological pathway.

Some neurotoxicologists are pursuing the hypothesis of a direct translocation pathway. Ultrafine particles may reach the brain through the olfactory bulb or by crossing the blood–brain barrier^{37,38,39} and proceed to harm some of its highly specialized cells: about 100 billion neurons and a few trillion glial support cells, including oligodendrocytes, astrocytes, and microglia.

Block, however, puts her money on the indirect route.^{40,41} “My lab studies how peripheral pulmonary damage impacts the brain through circulating serum factors that communicate a biological effect to the brain,” she explains. “We call this the lung–brain axis.”

Whether it is the direct or indirect route, at least some of the damage appears to be mediated by microglia, the brain’s resident immune cells. Both *in vivo* and *in vitro* studies suggest that air pollutants activate these cells and trigger inflammatory processes.⁴² In rats exposed to diesel exhaust, Block found the greatest response occurred in the brain regions with the highest microglial density.⁴⁰ Consistent with this observation, a recent study⁴³ implicated microglia in obesity-associated cognitive decline in mice.

“We’ve learned a great deal about the diverse roles of microglia and how they interact with the peripheral immune system,” says Block. “Since we know that they support normal learning and memory, I find it plausible that air pollution may impact the cognitive ability of healthy brains through its effect on microglia, but it hasn’t been proven yet.”

As the brain’s “Pac-Men,”⁴⁴ part of the everyday role of microglia is pruning synapses that are no longer needed. Synapses are the physical structures that neurons use to communicate with each other. With long-term exposure to air pollutants, Block thinks that peripheral signals could somehow reprogram microglia to drive chronic inflammation and oxidative stress. This may lead to a sustained impact on brain development and

function, explaining how air pollutants may increase the risk of neurodevelopmental and neurodegenerative diseases.

Block emphasizes that these are working hypotheses that have yet to be thoroughly tested in experimental models. Lucio Costa, a professor of environmental and occupational health sciences at the University of Washington, agrees with that assessment.

“Compared to metals and pesticides, studying the neurotoxic effects of air pollutants is a very young science,” Costa says. “I believe microglia play a central role and are the link between neurodevelopmental and neurodegenerative diseases, but there’s still much work to do to flesh out the mechanistic details that cause brain damage, and how peripheral inflammation contributes to it.”

Costa and Block have some ideas about where future studies might go. They both believe that brain images from large cohorts with long-term environmental exposure and cognitive test data^{45,46,47,48} provide valuable guidance for experimental work. They also think that serum samples can help in evaluating the role of peripheral damage.

What Is Next?

Thus far, most human studies have applied atmospheric models to data from U.S. EPA monitors to estimate personal pollutant exposures at locations of interest. Now that technology has reduced the price of some personal monitors to a few hundred dollars, researchers are now beginning to use these monitors to improve the precision of their exposure estimates.

“For PM_{2.5}, some of the consumer-grade devices on the market are showing pretty good agreement with the more expensive laboratory instruments,” says Kirsten Koehler, an associate professor of environmental health and engineering at The Johns Hopkins University. “But VOCs are even more heterogeneous and much trickier to measure [than PM_{2.5}], and ultrafine particles are still very challenging, too.”

In one of Koehler’s ongoing projects, investigators are deploying research- and consumer-grade monitors at public schools in the mid-Atlantic region to study the impact of renovation projects aimed at improving indoor air quality. Using before-and-after comparisons, the researchers will test if reduced indoor pollutant levels are associated with enhanced academic performance.

Encouraging findings from that kind of study have already been reported for 65 elementary schools in Texas, albeit without measured pollutants.⁴⁹ Following typical mold remediation and ventilation improvement projects, students scored higher on math and reading tests. The author concluded that such renovations “may be a more cost-effective way to improve standardized test scores than class size reductions.”

This finding was consistent with Allen’s calculations for the positive effect of higher ventilation rates on human productivity. As part of his group’s mission to promote the design of healthy buildings around the world, they are now enrolling hundreds of office workers from at least five countries for a longitudinal study. The team is using monitors to measure air pollutants in the office buildings and wearable devices to collect each worker’s health information. A newly developed smartphone app provides the participants with data summaries and reminders to complete cognitive surveys.

The interest in low-cost air quality monitors goes beyond academia. In California’s Imperial County, at the U.S./Mexico border, Paul English is helping residents keep tabs on their own exposures with one of the country’s largest community air monitoring networks.⁵⁰ About half the PM monitors are at public schools, linked to an online alert system that lets students shelter in place during poor air days, take different routes to school, or use inhalers. English, a senior science advisor at the California



Studies of mice suggest that brain regions with a high density of microglia may be especially sensitive to the pollutants in diesel exhaust.⁴⁰ The activation of microglia, the brain's resident immune cells, may trigger inflammatory processes and oxidative stress. Image: © Maren Winter/Shutterstock.

Department of Public Health, hopes this example will inspire similar projects in other communities.

This may be especially important for some of the 85,000 public schools in the United States that were recently analyzed for air pollution-related socioeconomic disparities.⁵¹ That study found that minority children in poor neighborhoods bear the brunt of exposures, with long-term implications for their future academic and earning potential.

Koehler applauds community monitoring efforts like California's. "It is the government's job to improve air quality at the state and national level, but I think it is great that the improved technology gives people actionable information for reducing their own exposures," she says.

Allen notes that the translation of public health findings into economic impacts is important because financial considerations drive many policy decisions. "When you put together all these different fields—toxicology, exposure assessment, epidemiology and health economics—that support a negative association of air pollution with human productivity and learning," he adds, "it becomes a powerful motivation for regulatory action."

Silke Schmidt, PhD, writes about science, health, and the environment from Madison, Wisconsin.

References

1. U.S. EPA (U.S. Environmental Protection Agency). 2011. *The Benefits and Costs of the Clean Air Act from 1990 to 2020*. <https://www.epa.gov/sites/production/files/2015-07/documents/summaryreport.pdf> [accessed 12 March 2019].
2. Kilian J, Kitazawa M. 2018. The emerging risk of exposure to air pollution on cognitive decline and Alzheimer's disease—evidence from epidemiological and animal studies. *Biomed J* 41(3):141–162, PMID: 30080655, <https://doi.org/10.1016/j.bj.2018.06.001>.
3. Ebenstein A, Lavy V, Roth S. 2016. The long-run economic consequences of high-stakes examinations: evidence from transitory variation in pollution. *Am Econ J Appl Econ* 8(4):36–65, <https://doi.org/10.1257/app.20150213>.
4. Graff Zivin J, Neidell M. 2018. Air pollution's hidden impacts. *Science* 359(6371):39–40, PMID: 29302005, <https://doi.org/10.1126/science.aap7711>.
5. U.S. EPA. Outdoor Air Quality Data: Air Data Basic Information. <https://www.epa.gov/outdoor-air-quality-data/air-data-basic-information> [accessed 18 March 2019].
6. U.S. EPA. 2018. Indoor Air Quality. Report on the Environment. 2018. <https://www.epa.gov/report-environment/indoor-air-quality> [accessed 11 Dec 2018].
7. McDonald BC, de Gouw JA, Gilman JB, Jathar SH, Akherati A, Cappa CD, et al. 2018. Volatile chemical products emerging as largest petrochemical source of urban organic emissions. *Science* 359(6377):760–764, PMID: 29449485, <https://doi.org/10.1126/science.aag0524>.
8. Health Effects Institute. 2018. State of Global Air 2018. <https://www.stateofglobalair.org/> [accessed 11 December 2018].
9. Zivin JG, Neidell M. 2012. The impact of pollution on worker productivity. *Am Econ Rev* 102(7):3652–3673, PMID: 26401055, <https://doi.org/10.1257/aer.102.7.3652>.
10. Chang T, Zivin JG, Gross T, Neidell M. 2016. Particulate pollution and the productivity of pear packers. *Am Econ J Econ Pol* 8(3):141–169, <https://doi.org/10.1257/pol.20150085>.
11. Chang TY, Zivin JG, Gross T, Neidell M, et al. 2019. The effect of pollution on worker productivity: evidence from call center workers in China. *Am Econ J Appl Econ* 11(1):151–172, <https://doi.org/10.1257/app.20160436>.
12. U.S. EPA. Outdoor Air Quality Data: Air Quality Index Daily Values Report. <https://www.epa.gov/outdoor-air-quality-data/air-quality-index-daily-values-report> [accessed 3 April 2019].

13. Heyes A, Neidell M, Saberian S. 2016. The effect of air pollution on investor behavior: evidence from the S&P 500. NBER working paper no. 22753. Cambridge, MA: National Bureau of Economic Research. <https://www.nber.org/papers/w22753> [accessed 11 December 2018].
14. Dohmen T, Falk A, Huffman D, Sunde U. 2010. Are risk aversion and impatience related to cognitive ability? *Am Econ Rev* 100(3):1238–1260, <https://doi.org/10.1257/aer.100.3.1238>.
15. Rabin M, Weizsäcker G. 2009. Narrow bracketing and dominated choices. *Am Econ Rev* 99(4):1508–1543, <https://doi.org/10.1257/aer.99.4.1508>.
16. Coudert V, Gex M. 2008. Does risk aversion drive financial crises? Testing the predictive power of empirical indicators. *J Empir Finance* 15(2):167–184, <https://doi.org/10.1016/j.jempfin.2007.06.001>.
17. Whaley RE. 2009. Understanding the VIX. *J Portfolio Manage* 35(3):98–105, <https://doi.org/10.3905/JPM.2009.35.3.098>.
18. Meyer S, Pagel M. Fresh air eases work: the effect of air quality on individual investor activity. New York, NY: Columbia University, Columbia University in the City of New York, Columbia Business School Research Archive. <https://www8.gsb.columbia.edu/researcharchive/articles/25560> [accessed 11 December 2018].
19. Allen JG, MacNaughton P, Satish U, Santanam S, Vallarino J, Spengler JD. 2016. Associations of cognitive function scores with carbon dioxide, ventilation, and volatile organic compound exposures in office workers: a controlled exposure study of green and conventional office environments. *Environ Health Perspect* 124(6):805–812, PMID: 26502459, <https://doi.org/10.1289/ehp.1510037>.
20. Lewis J, Baddeley AD, Bonham KG, Lovett D. 1970. Traffic pollution and mental efficiency. *Nature* 225(5227):95–97, <https://doi.org/10.1038/225095a0>.
21. Allen JG, MacNaughton P, Cedeno-Laurent JG, Cao X, Flanagan, S, Vallarino J, et al. 2018. Airplane pilot flight performance on 21 maneuvers in a flight simulator under varying carbon dioxide conditions. *J Expo Sci Environ Epidemiol*, PMID: 30089876, <https://doi.org/10.1038/s41370-018-0055-8>.
22. Satish U, Mendell MJ, Shekhar K, Hotchi T, Sullivan D, Streufert S, et al. 2012. Is CO₂ an indoor pollutant? Direct effects of low-to-moderate CO₂ concentrations on human decision-making performance. *Environ Health Perspect* 120(12):1671–1677, PMID: 23008272, <https://doi.org/10.1289/ehp.1104789>.
23. MacNaughton P, Pegues J, Satish U, Santanam S, Spengler J, Allen J. 2015. Economic, environmental and health implications of enhanced ventilation in office buildings. *Int J Environ Res Public Health* 12(11):14709–14722, PMID: 26593933, <https://doi.org/10.3390/ijerph121114709>.
24. Sunyer J, Suades-González E, García-Esteban R, Rivas I, Pujol J, Alvarez-Pedrerol M, et al. 2017. Traffic-related air pollution and attention in primary school children: short-term association. *Epidemiology* 28(2):181–189, PMID: 27922536, <https://doi.org/10.1097/EDE.0000000000000603>.
25. Perera FP, Rauh V, Whyatt RM, Tsai W-Y, Tang D, Diaz D, et al. 2006. Effect of prenatal exposure to airborne polycyclic aromatic hydrocarbons on neurodevelopment in the first 3 years of life among inner-city children. *Environ Health Perspect* 114(8):1287–1292, PMID: 16882541, <https://doi.org/10.1289/ehp.9084>.
26. Marcotte DE. 2017. Something in the air? Air quality and children's educational outcomes. *Econ Educ Rev* 56:141–151, <https://doi.org/10.1016/j.econeducrev.2016.12.003>.
27. Bharadwaj P, Gibson M, Zivin JG, Neilson C. 2017. Gray matters: fetal pollution exposure and human capital formation. *J Assoc Environ Resour Econ* 4(2):505–542, <https://doi.org/10.1086/691591>.
28. Wang P, Tuvblad C, Younan D, Franklin M, Lurmann F, Wu J, et al. 2017. Socioeconomic disparities and sexual dimorphism in neurotoxic effects of ambient fine particles on youth IQ: a longitudinal analysis. *PLoS One* 12(12): e0188731, PMID: 29206872, <https://doi.org/10.1371/journal.pone.0188731>.
29. Costa LG, Cole TB, Coburn J, Chang Y-C, Dao K, Roque P, et al. 2014. Neurotoxins are in the air: convergence of human, animal, and *in vitro* studies on the effects of air pollution on the brain. *Biomed Res Int* 2014:736385, PMID: 24524086, <https://doi.org/10.1155/2014/736385>.
30. Flores-Pajot M-C, Ofner M, Do MT, Lavigne E, Villeneuve PJ. 2016. Childhood autism spectrum disorders and exposure to nitrogen dioxide, and particulate matter air pollution: a review and meta-analysis. *Environ Res* 151:763–776, PMID: 27609410, <https://doi.org/10.1016/j.envres.2016.07.030>.
31. Isen A, Rossin-Slater M, Walker WR. 2017. Every breath you take—every dollar you'll make: the long-term consequences of the Clean Air Act of 1970. *J Polit Econ* 125(3):848–902, <https://doi.org/10.1086/691465>.
32. Power MC, Adar SD, Yanosky JD, Weuve J. 2016. Exposure to air pollution as a potential contributor to cognitive function, cognitive decline, brain imaging, and dementia: a systematic review of epidemiologic research. *Neurotoxicology* 56:235–253, PMID: 27328897, <https://doi.org/10.1016/j.neuro.2016.06.004>.
33. Zhang X, Chen X, Zhang X. 2018. The impact of exposure to air pollution on cognitive performance. *Proc Natl Acad Sci USA* 115(37):9193–9197, PMID: 30150383, <https://doi.org/10.1073/pnas.1809474115>.
34. Calderón-Garcidueñas L, Azzarelli B, Acuna H, Garcia R, Gambling TM, Osnaya N, et al. 2002. Air pollution and brain damage. *Toxicol Pathol* 30(3):373–389, PMID: 12051555, <https://doi.org/10.1080/01926230252929954>.
35. Calderón-Garcidueñas L, González-Maciel A, Reynoso-Robles R, Kulesza RJ, Mukherjee PS, Torres-Jardón R, et al. 2018. Alzheimer's disease and alpha-synuclein pathology in the olfactory bulbs of infants, children, teens and adults ≤40 years in Metropolitan Mexico City. APOE4 carriers at higher risk of suicide accelerate their olfactory bulb pathology. *Environ. Res* 166:348–362, PMID: 29935448, <https://doi.org/10.1016/j.envres.2018.06.027>.
36. Calderón-Garcidueñas L, Mukherjee PS, Kulesza RJ, Torres-Jardón R, Hernández-Luna J, Ávila-Cervantes R, et al. 2019. Mild cognitive impairment and dementia involving multiple cognitive domains in Mexican urbanites. *J Alzheimers Dis* 68(3):1113–1123, PMID: 30909241, <https://content.iospress.com/articles/journal-of-alzheimers-disease/jad181208>.
37. Oberdörster G, Sharp Z, Atudorei V, Elder A, Gelein R, Kreyling W, et al. 2004. Translocation of inhaled ultrafine particles to the brain. *Inhal Toxicol* 16(6–7):437–445, PMID: 15204759, <https://doi.org/10.1080/08958370490439597>.
38. Block ML, Calderón-Garcidueñas L. 2009. Air pollution: mechanisms of neuroinflammation and CNS disease. *Trends Neurosci* 32(9):506–516, PMID: 19716187, <https://doi.org/10.1016/j.tins.2009.05.009>.
39. Maher BA, Ahmed IAM, Karloukovi V, MacLaren DA, Foulds PG, Allsop D, et al. 2016. Magnetite pollution nanoparticles in the human brain. *Proc Natl Acad Sci USA* 113(39):10797–10801, PMID: 27601646, <https://doi.org/10.1073/pnas.1605941113>.
40. Levesque S, Taetsch T, Lull ME, Kodavanti U, Stadler K, Wagner A, et al. 2011. Diesel exhaust activates and primes microglia: air pollution, neuroinflammation, and regulation of dopaminergic neurotoxicity. *Environ Health Perspect* 119(8):1149–1155, PMID: 21561831, <https://doi.org/10.1289/ehp.1002986>.
41. Mumaw CL, Levesque S, McGraw C, Robertson S, Lucas S, Staffinger JE, et al. 2016. Microglial priming through the lung-brain axis: the role of air pollution-induced circulating factors. *FASEB J* 30(5):1880–1891, PMID: 26864854, <https://doi.org/10.1096/fj.201500047>.
42. Block ML, Elder A, Auten RL, Bilbo SD, Chen H, Chen J-C, et al. 2012. The outdoor air pollution and brain health workshop. *Neurotoxicology* 33(5):972–984, PMID: 22981845, <https://doi.org/10.1016/j.neuro.2012.08.014>.
43. Cope EC, LaMarca EA, Monari PK, Olson LB, Martinez S, Zych AD, et al. 2018. Microglia play an active role in obesity-associated cognitive decline. *J Neurosci* 38(41):8889–8904, PMID: 30201764, <https://doi.org/10.1523/JNEUROSCI.0789-18.2018>.
44. Stevens B. 2015. Big idea: the brain's best kept secret. *Popular Science*, Health section, online edition. 22 December 2015. <https://www.popsci.com/big-idea-brains-best-kept-secret> [accessed 11 December 2018].
45. Chen J-C, Wang X, Wellenius GA, Serre ML, Driscoll I, Casanova R, et al. 2015. Ambient air pollution and neurotoxicity on brain structure: evidence from Women's Health Initiative Memory Study. *Ann Neurol* 78(3):466–476, PMID: 26075655, <https://doi.org/10.1002/ana.24460>.
46. Wilker EH, Preis SR, Beiser AS, Wolf PA, Au R, Kloog I, et al. 2015. Long-term exposure to fine particulate matter, residential proximity to major roads and measures of brain structure. *Stroke* 46(5):1161–1166, PMID: 25908455, <https://doi.org/10.1161/STROKEAHA.114.008348>.
47. Wilker EH, Martinez-Ramirez S, Kloog I, Schwartz J, Mostofsky E, Koutrakis P, et al. 2016. Fine particulate matter, residential proximity to major roads, and markers of small vessel disease in a memory study population. *J Alzheimers Dis* 53(4):1315–1323, PMID: 27372639, <https://doi.org/10.3233/JAD-151143>.
48. Power MC, Lamichhane AP, Liao D, Xu X, Jack CR, Gottesman RF, et al. 2018. The association of long-term exposure to particulate matter air pollution with brain MRI findings: the ARIC study. *Environ Health Perspect* 126(2):027009, PMID: 29467108, <https://doi.org/10.1289/EHP2152>.
49. Tafford TM. 2015. Indoor air quality and academic performance. *J Environ Econ Manage* 70:34–50, <https://doi.org/10.1016/j.jeem.2014.11.002>.
50. English PB, Olmedo L, Bejarano E, Lugo H, Murillo E, Seto E, et al. 2017. The Imperial County Community Air Monitoring Network: a model for community-based environmental monitoring for public health action. *Environ Health Perspect* 125(7):074501, PMID: 28886604, <https://doi.org/10.1289/EHP1772>.
51. Grineski SE, Collins TW. 2018. Geographic and social disparities in exposure to air neurotoxins at U.S. public schools. *Environ Res* 161:580–587, PMID: 29245126, <https://doi.org/10.1016/j.envres.2017.11.047>.
52. Riesenber DE, Arehart-Treichel J. 1986. "Sick building" syndrome plagues workers, dwellers. *JAMA* 255(22):3063, PMID: 3702102, <https://doi.org/10.1001/jama.1986.03370220021005>.
53. USGBC (U.S. Green Building Council). 2014. LEED v4 User Guide. Washington DC: U.S. Green Building Council. <http://www.usgbc.org/resources/leed-v4-user-guide> [accessed 4 March 2019].